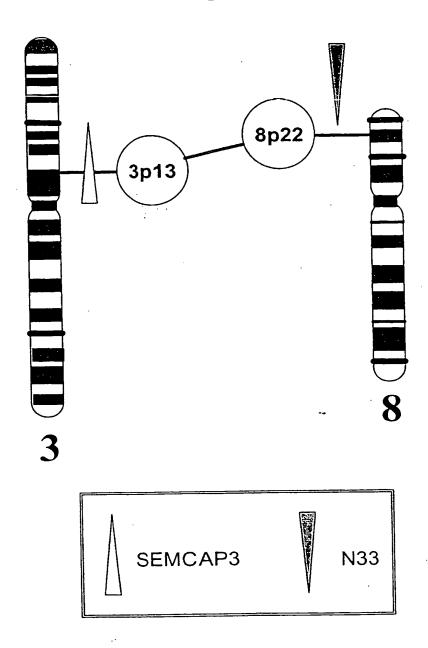
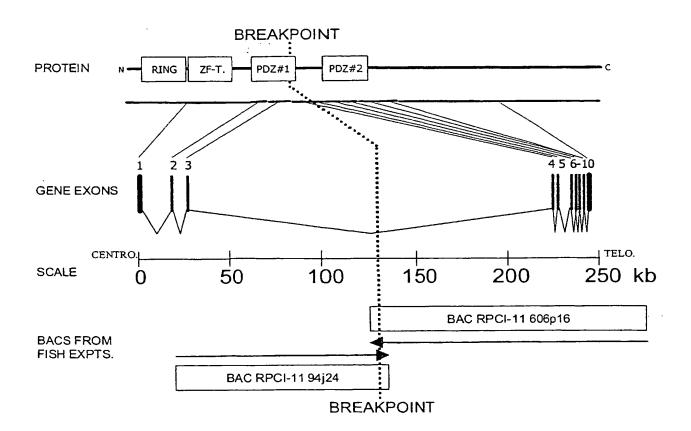
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Figure 1



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Figure 3

1	AAAACTTCCC	CGGGTAGATT	CACCCACCGG	TCCTGGAAAC	CTGCTAAATC	CTGAAGGTTC
61	ACAGAACCTC	TGGTCAGAAC	TGAAGTTGCA	GCCGGAGCTT	CCCGCAGGCT	CTGTAACTTT
121	CCCTGGAATG	AATAAATAA	ATAAAGACCG	TAAGTGCTGA	GATAGCGGGC	CCCAAGATAT
181	TTTTAGTCCT	CTGCAATCAG	CCACTAGAGG	AAGGGGGAGG	GAGAAGGGAG	TAAAAAAGTT
241	TTGATCCGTT	CGGGAAGGGG	CTCGAAGAGA	ACCCTTGGGA	GAAAGCAGTA	GCCTCAGCTC
301	CAAACTCAGC	GAGCTTTTCT	CGGCTGGCGT	TTTGTCTCCT	ATAGCGTAGA	CTGTAAGAGA
361	ACAGAAAGGA	GTTTCCCGAG	AAGATTCAGG	CTGGCGTCCT	GGGCTGGCCC	GTCCCTTCTG
421	GCGAGCCTCA	GTGTCCTCCC	ACGCGCTTCT	GCCTTCCAGC	CTCCTCCCTT	TTTCGGGGGG
481	CTGGCGGGAG	GCATCCAAGG	CACGATGTAT	GTGCGCTCGC	GCTCGCGCAA	ATACGGCCGG
541	AGGAGTCCTG	TTCCTCGGGC	ATTTTCCGAG	GAAGTCTGGA	TCAATTAGGC	TCAGTCCGGG
601	GAGAGCCAGC	GAGCGCGCGG	GCGGCGTAGC	CGGCCTGTCT	GGGCCGCCTC	GTGGGGAGGG
661	AGGGGGCGCC	CGGCCGCCCG	GCGGCGACCC	CGGGGCCTGG	CCGCCACCAT	GGGCTTCGAG
721	CTGGACCGCT	TCGACGCCGA	CGTGGACCCG	GACCTGAAGT	GCGCGCTGTG	CCACAAGGTC
781	CTGGAGGACC	CGCTGACCAC	GCCGTGCGGC	CACGTCTTCT	$\mathop{\mathtt{GCGCCGGCTG}}_{\cdot}$	CGTGCTGCCC
841	TGGGTGGTGC	AGGAGGGCAG	CTGCCCGGCG	CGCTGCCGCG	GTCGCCTGTC	GGCCAAAGAG
901	CTCAACCACG	TCCTGCCGCT	CAAGCGCCTT	ATCCTCAAGC	TGGACATCAA	GTGCGCGTAC
961	GCGACGCGCG	GCTGCGGCCG	GGTGGTCAAG	CTGCAGCAGC	TGCCGGAGCA	CCTCGAGCGC
1021	TGCGACTTCG	CGCCCGCGCG	CTGTCGCCAC	GCGGGTTGCG	GCCAGGTGCT	GCTGCGGCGC
1081	GACGTGGAGG	CGCACATGCG	CGACGÇGTGC	GACGCGCGGC	CAGTGGGCCG	CTGCCAGGAG
1141	GGCTGCGGGC	TACCCTTGAC	GCACGGCGAG	CAGCGCGCGG	GCGGCCACTG	CTGCGCGCGA
1201	GCGCTGCGGG	CGCACAACGG	CGCGCTCCAG	GCCCGCCTGG	GCGCGCTGCA	CAAGGCGCTC
1261	AAGAAGGAGG	CGCTGCGCGC	TGGGAAGCGC	GAGAAGTCGC	TGGTGGCCCA	GCTGGCCGCG
1321	GCGCAGCTTG	AGCTGCAGAT	GACCGCGCTG	CGĊTACCAGA	AGAAATTCAC	CGAATACAGC
1381	GCGCGCCTCG	ACTCGCTCAG	CCGCTGCGTG	GCCGCGCCGC	CCGGCGGCAA	GGGCGAAGAA
1441	ACCAAAAGTC	TGACTCTTGT	CCTGCATCGG	GACTCCGGCT	CCCTGGGATT	CAATATTATT
1501	GGTGGCĆGGC	CGAGTGTGGA	TAACCACGAT	GGATCATCCA	GTGAAGGAAT	CTTTGTATCC
1561	AAGATAGTTG	ACAGTGGGCC	TGCAGCCAAG	GAAGGAGGCC	TGCAAATTCA	TGACAGGATT
1621	ATTGA <u>GG</u> TCA	ACGGCAGAGA	CTTATCCAGA	GCAACTCATG	ACCAGGCTGT	GGAAGCTTTC
1681	AAGACAGCCA	AGGAGCCCAT	AGTGGTGCAG	GTGTTGAGAA	GAACACCAAG	GACCAAAATG
1741	TTCACGCCTC	CATCAGAGTC	TCAGCTGGTG	GACACGGGAA	CCCAAACCGA	CATCACCTTT
1801	GAACATATCA	TGGCCCTCAC	TAAGATGTCC	TCTCCCAGCC	CACCCGTGCT	GGATCCCTAT
1861	CTCTTGCCAG	AGGAGCATCC	CTCAGCCCAT	GAATACTACG	ATCCAAATGA	CTACATTGGA
1921	GACATCCATC	AGGAGATGGA	CAGGGAGGAG	CTGGAGCTGG	AGGAAGTGGA	CCTCTACAGA
1981	ATGAACAGCC	AGGACAAGCT	GGGCCTCACT	GTGTGCTACC	GGACGGACGA	TGAAGACGAC

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2041	ATTGGGATTT	ATATCAGTGA	GATTGACCCT	AACAGCATTG	CAGCCAAGGA	TGGGCGCATC
2101	CGAGAAGGAG	ACCGCATTAT	CCAGATTAAT	GGGATAGAGG	TGCAGAACCG	TGAAGAGGCT
2161	GTGGCTCTTC	TAACCAGTGA	AGAAAATAAA	AACTTTTCAT	TGCTGATTGC	AAGGCCTGAA
2221	CTCCAGCTGG	ATGAGGGCTG	GATGGATGAT	GACAGGAACG	ACTTTCTGGA	TGACCTGCAC
2281	ATGGACATGC	TGGAGGAGCA	GCACCACCAG	GCCATGCAAT	TCACAGCTAG	CGTGCTGCAG
2341	CAGAAGAAGC	ACGACGAAGA	CGGTGGGACC	ACAGATACAG	CCACCATCTT	GTCCAACCAG
2401	CACGAGAAGG	ACAGCGGTGT	GGGGCGGACC	GACGAGAGCA	CCCGTAATGA	CGAGAGCTCG
2461	GAGCAAGAGA	ACAATGGCGA	CGACGCCACC	GCATCCTCCA	ACCCGCTGGC	GGGGCAGAGG
2521	AAGCTCACCT	GCAGCCAGGA	CACCTTGGGC	AGCGGCGACC	TGCCCTTCAG	CAACGAGTCT
2581	TTCATTTCGG	CCGACTGCAC	GGACGCCGAC	TACCTGGGGA	TCCCGGTGGA	CGAGTGCGAG
2641	CGCTTCCGCG	AGCTCCTGGA	GCTCAAGTGC	CAGGTGAAGA	GCGCCACCC	TTACGGCCTG
2701	TACTACCCTA	GCGGCCCCT	GGACGCCGGC	AAGAGTGACC	CTGAGAGCGT	GGACAAGGAG
2761	CTGGAGCTGC	TGAACGAAGA	GCTGCGCAGC	ATCGAGCTGG	AGTGCCTGAG	CATCGTGCGC
2821	GCCCACAAGA	TGCAGCAGCT	CAAGGAGCAG	TACCGCGAGT	CCTGGATGCT	GCACAACAGC
2881	GGCTTCCGCA	ACTACAACAC	CAGCATCGAC	GTGCGCAGAC	ACGAGCTCTC	AGATATCACC
2941	GAGCTCCCGG	AGAAATCCGA	CAAGGACAGC	TCGAGCGCCT	ACAACACAGG	CGAGAGCTGC
3001	CGCAGCACCC	CGCTCACCCT	GGAGATCTCC	CCCGACAACT	CCTTGAGGAG	AGCGGCGGAG
3061	GGCATCAGCT	GCCCGAGCAG	CGAAGGGGCT	GTGGGGACCA	CGGAAGCCTA	CGGGCCAGCC
3121	TCCAAGAATC	TGCTCTCCAT	CACGGAAGAT	CCCGAAGTGG	GCACCCCTAC	CTATAGCCCG
3181	TCCCTGAAGG	AGCTGGACCC	CAACCAGCCC	CTGGAAAGCA	AAGAGCGGAG	AGCCAGCGAC
3241	GGGAGCCGGA	GCCCCACGCC	CAGCCAGAAG	CTGGGCAGCG	CCTACCTGCC	CTCCTATCAC
3301	CACTCCCCAT	ACAAGCACGC	GCACATCCCG	GCGCACGCCC	AGCACTACCA	GAGCTACATG
3361	CAGCTGATCC	AGCAGAAGTC	GGCCGTGGAG	TACGCGCAAA	GCCAGATGAG	CCTGGTGAGC
3421	ATGTGCAAGG	ACCTGAGCTC	TCCCACCCCG	TCGGAGCCGC	GCATGGAGTG	GAAGGTGAAG
3481	ATCCGCAGCG	ACGGGACGCG	CTACATCACC	AAGAGGCCCG	TGCGGGACCG	CCTGCTGCGG
3541	GAGCGCGCCC	TGAAGATCCG	GGAAGAGCGC	AGCGGCATGA	CCACCGACGA	${\tt CGACGCGGTG}_{.}$
3601	AGCGAGATGA	AGATGGGGCG	CTACTGGAGC	AAGGAGGAGA	GGAAGCAGCA	CCTGGTGAAG
3661	GCCAAGGAGC	AGCGGCGGCG	GCGCGAGTTC	ATGATGCAGA	GCAGGTTGGA	TTGTCTCAAG
3721	GAGCAGCAAG	CAGCCGATGA	CAGGAAGGAG	ATGAACATTC	TCGAACTGAG	CCACAAAAAG
3781	ATGATGAAGA	AGAGGAATAA	GAAAATCTTC	GATAACTGGA	TGACGATCCA	AGAACTCTTA
3841	ACCCACGGCA	CAAAATCCCC	GGACGGCACT	AGAGTATACA	ATTCCTTCCT	ATCGGTGACT
3901	ACTGTA <u>TAA</u> T	TTTCACTTCT	GCATTATGTA	CATAAAGGAG	ACCACTACCA	CTGGGGTAGA
3961	AATTCCTGCC	TCGTTCAATG	CGGCAAGTTT	TTGTATATAA	GATAAGTACG	GTCTTCATGT
4021	TTATAGTCCA	AATTTGCAAA	CCCTACAACT	CTGGGTGTCA	TAGGTCTATT	TTAAGGGAAG
4081	AGAGAGAAAA	ACACCCTTAC	TATCTTGGAA	GGCAATATTA	ACAAACAGAG	CTTTTTTCAA
4141	ATAGCAATTG	TACTTTTCTA	CCTGTACCCT	TTTACATAAA	GTGTTTAAAT	TTCAGAAAGA

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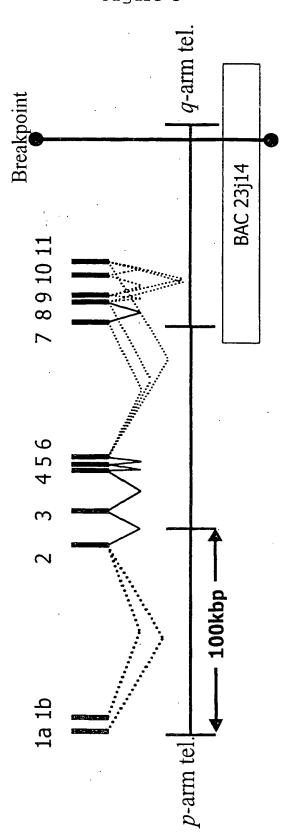
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4321	GAACCCTATT	TTATAATGGT	ACGTTACTGA	ATGTGTTTCA	TATGCGTGAC	CGTTAAGATA
4381	TTATCATTTA	GGTGAAGGTT	TCAACTCAAA	ACCACCCAAC	CCGGTGGTTA	ACGATTTAAT
4441	ACATATAACC	AAACCGGCAG	CGTTTAGAGT	TGGGATATAC	ATTTAAACAT	TTTCCTGGTT
4501	AAGGTTCCCA	AGAGAGTGTA	AAGGTTTTAG	CAGAAAGCAA	AATATCTTGC	ATCTTTATGG
4561	AAGTTTAAAG	CATGTTTGCA	AATATTGCAG	CCCATTGAAA	GAATTTGCAT	GTACAGGAAA
4621	GTTGTGGATG	GAGACGGTTT	GTGGAATTTT	AAGTGCTCAT	TGTAGTAAAC	TTTTGCTTTG
4681	TAGATTTGAA	GGTACAGACT	TATACAGGCA	AGTTCACAAA	ATCATGATTA	GTTACAAACA
4741	GTAAAATGAA	GTTAAAATAA	ATTATTATTT	TCT		

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Figure 4

1	MGFELDRFDG	DVDPDLKCAL	CHKVLEDPLT	TPCGHVFCAG	CVLPWVVQEG	SCPARCRGRL
61	SAKELNHVLP	LKRLILKLDI	KCAYATRGCG	RVVKLQQLPE	HLERCDFAPA	RCRHAGCGQV
121	LLRRDVEAHM	RDACDARPVG	RCQEGCGLPL	THGEQRAGGH	CCARALRAHN	GALQARLGAL
181	HKALKKEALR	AGKREKSLVA	QLAAAQLELQ	MTALRYQKKF	TEYSARLDSL	SRCVAAPPGG
241	KGEETKSLTL	VLHRDSGSLG	FNIIGGRPSV	DNHDGSSSEG	IFVSKIVDSG	PAAKEGGLQI
301	HDRIIEVNGR	DLSRATHDQA	VEAFKTAKEP	IVVQVLRRTP	RTKMFTPPSE	SQLVDTGTQT
361	DITFEHIMAL	TKMSSPSPPV	LDPYLLPEEH	PSAHEYYDPN	DYIGDIHQEM	DREELELEEV
421	DLYRMNSQDK	LGLTVCYRTD	DEDDIGIYIS	EIDPNSIAAK	DGRIREGDRI	IQINGIEVQN
481	REEAVALLTS	EENKNFSLLI	ARPELQLDEG	WMDDDRNDFL	DDLHMDMLEE	QHHQAMQFTA
541	SVLQQKKHDE	DGGTTDTATI	LSNQHEKDSG	VGRTDESTRN	DESSEQENNG	DDATASSNPL
601	AGQRKLTCSQ	DTLGSGDLPF	SNESFISADC	TDADYLGIPV	DECERFRELL	ELKCQVKSAT
661	PYGLYYPSGP	LDAGKSDPES	VDKELELLNE	ELRSIELECL	SIVRAHKMQQ	LKEQYRESWM
721	LHNSGFRNYN	TSIDVRRHEL	SDITELPEKS	DKDSSSAYNT	GESCRSTPLT	LEISPDNSLR
781	RAAEGISCPS	SEGAVGTTEA	YGPASKNLLS	ITEDPEVGTP	TYSPSLKELD	PNQPLESKER
841	RASDGSRSPT	PSQKLGSAYL	PSYHHSPYKH	АНІРАНАОНУ	QSYMQLIQQK	SAVEYAQSQM
901	SLVSMCKDLS	SPTPSEPRME	WKVKIRSDGT	RYITKRPVRD	RLLRERALKI	REERSGMTTD
961	DDAVSEMKMG	RYWSKEERKQ	HLVKAKEQRR	${\tt RREFMMQSRL}$	DCLKEQQAAD	DRKEMNILEL
1021	SHKKMMKKRN	KKIFDNWMTI	QELLTHGTKS	PDGTRVYNSF	LSVTTV	

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Figure 6

la

1b

2-6

These exons have been joined together as they are always spliced in this way.

aatcttttagctgaaaaagtagagcagctgatggaatggagttccagacgctcaatctt ccgaatgaatggtgataaattccgaaaatttataaaggcaccacctcgaaactattcca tgattgttatgttcactgctcttcagcctcagcggcagtgttctgtgtgcaggcaagct aatgaagaatatcaaatactggcgaactcctggcgctattcatctgctttttgtaacaa gctcttcttcagtatggtggactatgatgaggggacagacgtttttcagcagctcaaca tgaactctgctcctacattcatgcattttcctccaaaaggcagacctaagagagctgat acttttgacctccaaagaattggatttgcagctgagcaactagcaaagtggattgctga cagaacggatgttcatattcgggttttcagaccaccaactactctggtaccattgctt tggccctgttagtgtcgcttgttggaggtttgctttatttgagaaggaacaacttggag ttcatctataacaagactggttgggccatggtgtctctgtgtatagtctttgctatgac ttctggccagatgtggaaccatatcgtggaccaccacacaaaaggacaagtg

- agctacattcatgggagcagccaggctcagtttgtggcagaatcacacattattctggtactga
- atgccgctatcaccatggggatggttcttctaaatgaagcagcaacttcgaaaggcgatgttggaaaaagacgga

8+

This is identical to 8 except a cryptic splice acceptor upstream is employed.

tttaaccattctggaacattgtgttcagagccagaaaaattaatagattttattcacat ctatgtctacggcttccttgacaactactgcagatgccgctatcaccatggggatggttcttctaaatgaagcagcaacttcgaaaggcgatgttggaaaaagacgga

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- 9
 taatttgcctagtgggattgggcctggtggtcttcttcttcagttttctactttcaata
 tttcgttccaagtaccacggctatccttatag
- 10 tgatctggactttgagtgagaagatgtgatttggaccatggcacttaaaaactctataa cctcag
- 11 ctttttaattaaatgaagccaagtgggatttgcataaagtgaatgtttaccatgaagat aaactgttcctgactttatactattttgaattc

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Figure 7

Alternative start exons

1a:

MEWSSRRSIFRMNGDKFRKFIKAPPRNYS..... (encoded by exon 2).

1b:

MGARGAPSRRRQAGRRLRYLPTGSFPFLLLLLLLCIQLGGGQKKKENLLAEKVEQLMEW SSRRSIFRMNGDKFRKFIKAPPRNYS......

Transcript options

2-6, 7, 8, 9, 10, 11

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2-6,7,8,9,11

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2-6,11

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EQLAKWIADRTDVHIRVFRPPNYSGTIALALLVSLVGGLLYLRRNNLEFIYNKTGWAMV SLCIVFAMTSGQMWNHIRGPPYAHKNPHNGQVLFN

2-6,7,8,11

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2-6,8+,9,11

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2-6,8+,11

aatcttttagctgaaaaagtagagcagctgatggaatggagttccagacgctcaatctt ccgaatgaatggtgataaattccgaaaatttataaaggcaccacctcgaaactattcca tgattgttatgttcactgctcttcagcctcagcggcagtgttctgtgtgcaggcaagct aatgaagaatatcaaatactggcgaactcctggcgctattcatctgctttttgtaacaa gctcttcttcagtatggtggactatgatgaggggacagacgtttttcagcagctcaaca tgaactctgctcctacattcatgcattttcctccaaaaggcagacctaagagagctgat acttttgacctccaaagaattggatttgcagctgagcaactagcaaagtggattgctga cagaacggatgttcatattcgggttttcagaccacccaactactctggtaccattgctt tggccctgttagtgtcgcttgttggaggtttgctttatttgagaaggaacaacttggag ttcatctataacaagactggttgggccatggtgtctctgtgtatagtctttgctatgac ttctggccagatgtggaaccatatccgtggacctccatatgctcataagaacccacaca atggacaagtgtttaaccattctggaacattgtgttcagagccagaaaaattaatagat tttattcacatctatgtctacggcttccttgacaactactgcagatgccgctatcacca tggggatggttcttctaaatgaagcagcaacttcgaaaggcgatgttggaaaaagacgg actttttaattaaatgaagccaagtgggatttgcataaagtgaatgtttaccatgaaga taaactgttcctgactttatactattttgaattc

(MGARGAPSRRRQAGRRLRYLPTGSFPFLLLLLLCIQLGGGQKKKENLLAEKVEQL) M EWSSRRSIFRMNGDKFRKFIKAPPRNYSMIVMFTALQPQRQCSVCRQANEEYQILANSW RYSSAFCNKLFFSMVDYDEGTDVFQQLNMNSAPTFMHFPPKGRPKRADTFDLQRIGFAA EQLAKWIADRTDVHIRVFRPPNYSGTIALALLVSLVGGLLYLRRNNLEFIYNKTGWAMV SLCIVFAMTSGQMWNHIRGPPYAHKNPHNGQVFNHSGTLCSEPEKLIDFIHIYVYGFLD NYCRCRYHHGDGSSK

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Figure 8

IAG2_HUMAN N33_HUMAN DROSCG7830 Celegans_g304348 Yeast_Ost3p Yeast_Ost6p	MAARWRFWCVSVTMVVALLIVCDVPSASA MGARGAPSRRRQAGRRLRYLPTGSFPFLLLLLLLCIQLGGG
IAG2_HUMAN N33_HUMAN DROSCG7830 Celegans_g304348 Yeast_Ost3p Yeast_Ost6p	QRKKE-MVLSEKVSQEMEWTNKRPVIRMNGDKFRRLVKAPE QKKKE-NLLAEKVEQEMEWSSRRSIFRMNGDKFRKFIKAPE SKSKTGLSLSEKVQNEVDMNAKKPLLRFNGPKFREYVKSAE QQTLEDKVQNEVDLTSRQSIVKFNMDKWKTLVRMQE STHPALAMSSNRLLKEANKSPKKIIPLKDSSFENILAE QKSTATASHNIDDILQLKDDTGVITVTADNYPLLSRGVE
IAG2_HUMAN N33_HUMAN DROSCG7830 Celegans_g304348 Yeast_Ost3p Yeast_Ost6p	RYSVIVMFIZLQLHROGVVOKQADEEFQILANGWRYSSRYSMITVMFIZLQPQROGSVORQANEEYQILANGWRYSSRYSMITVMLIZALAPSROGQICRHAHDEFAIVENGYRFSSRYSMITVMFIZLSPGVQCPICKPAYDEFMIVENGHRYTS PHENAYIVALFIZTAPEIGESLOLELESEYDTIVASWFDDH GYFNILYITMRGTNSNGMSCQLCHDFEKTYHAVADVIRSQA CYST.
IAG2_HUMAN N33_HUMAN DROSCG7830 Celegans_g304348 Yeast_Ost3p Yeast_Ost6p	AFTNRIFFAMVOFDEGSDVEOMLNMSAFTF AFCNKLARSMVEYDEGTDVEOQLNVNSAFTF TYSNKLEBAMVOFDDGSEVEOLLRLYTAFVF SEGDRRKVEEGIVOYEDAPQIFOQMNLYTAFIL PDAKSSNSDTSIEFTKVNLEDPSKTIPKAFOFFQLNVVERL PQSLNLEFTVOVNEVPQLVKDLKLQNVEHL
IAG2_HUMAN N33_HUMAN DROSCG7830 Celegans_g304348 Yeast_Ost3p Yeast_Ost6p	INEPAK-GKPKRGDTYELQVRGFSAEQIARWIADR MHEPPK-GRPKRADTFDLQRIGFAAEQLAKWIADR MHEPAK-GKPKGADTMDIHRVGFAADSIAKFVAER YHEGPKLGAKKRPEQMDFQRQGFDADAIGRFVADQ FIEKPNSPSILDHSVISISTDTGSERMKQIIQAIKQF VVYPPAESNKQSQFEWKTSPFYQYSLVPENAENTLQFGDFL
IAG2_HUMAN N33_HUMAN DROSCG7830 Celegans_g304348 Yeast_Ost3p Yeast_Ost6p	-TDVNIRVIRPENYAGPLMLGLLLAVIGGLVYLRRSNMEFTDVHIRVFREDNYSGTIALALLVSLVGGLLYLRRNNTEFTDITIRIFREDNYSGTVAMITLVALVGSFLYIRRNNTEFTEVHVRVIRPENYTAPVVIALFVALLLGMLYMKRNSEDFSQVNDFSLHLEMDWTPIITSTIITFITVLLFKKQSKEMFS AKILNISITVEQAFNVQEFVYYFVACMVVFIFIKKVIEPKV

Yeast Ost6p.

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-LFNKTGWAFAALCFVLAMTSCOMWHINGPEYAHKNPHTG
-IYNKTGWAMVSLCIVFAMTSCOMWHINGPEYAHKNPHNG
-LYNKNLWGAIAVFFCFAMISCOMWHINGPELVHKS-QNG
-LFNRTVWGFVCLAITFIFMSCOMWNHUNGPEFMITNPNTK IAG2 HUMAN N33 HUMAN DROS. CG7830 Celegans g304348 IISSRIINATLSTFFIICMI AYMFTOTENTOLAGVGPKGE Yeast_Ost3p TNKWKLFSMILSLGILLPSITEYKFVEMNAIEFIARDAKN-Yeast Ost6p CCCCC*******TM 2***** IAG2 HUMAN HVNYIHGSSQA@FVA@THIVLLFNGGVTLGMVLLCEAATSD QVSYIHGSSQA FVA HSHIILVLNAAITMGMVLLNEAATSK N33 HUMAN GVAYIHGSSQGOLVVETYIVMFLNAMIVLGMILLIESGTPK EPSFIHGSTQFOLIAETYIVGLLYALIAIGFICVNEAADQS DROS._CG7830 Celegans_g304348 VMYFLPNEFQHÖFAIÖTQVMVLIYGTLAALVVVLVKGIQFL Yeast_Ost3p Yeast Ost6p RIMYFSGGSGW@FGIBIFSVSLMYIVMSALSVLLIYVPKIS ******TM 3*****CCCCCCC IAG2_HUMAN MDIGKR-----KIMCVAGIGLVVL NAMUH EEN GDVGKR------RIICLVGLGLVVFFFSFLL DROS._CG7830 AHN-KN------FIMAMTGLVLLTVESFLL Celegans g304348 NSKDRKNAGKKLNPLSLLNIPTNTLAIAGLVCICVERSFLL Yeast Ost3p RSHLYP-----ETKKAYFIDAILASFCALFIYVEEAALT CVSEKMR------GLLSSFLACVLFYFFSYFI Yeast_Ost6p ccccccccccccccccccc****TM 4**** TF (3) IAG2 HUMAN N33 HUMAN DROS._CG7830 Celegans g304348 Yeast Ost3p

FLIK (2)

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Figure 9

C-termini of N33 splice forms

N33_67891011_TranslatedLonge N33_67891011_TranslatedLon N33_678911_TranslatedLongest N33_6811_TranslatedLonge N33_68+911_TranslatedLonge N33_68+11_TranslatedLonge	LVSLVGGLLYLRRNNLEFIYNKTEKKNYST TYFKKTSIQMWNHIRGPPY LVSLVGGLLYLRRNNLEFIYNKTEKKNYST TYFKKTSIQMWNHIRGPPY LVSLVGGLLYLRRNNLEFIYNKTEKKNYST TYFKKTSIQMWNHIRGPPY LVSLVGGLLYLRRNNLEFIYNKTEKKNYST TYFKKTSIQMWNHIRGPPY LVSLVGGLLYLRRNNLEFIYNKTEKKNYST TYFKKTSIQMWNHIRGPPY LVSLVGGLLYLRRNNLEFIYNKTEKKNYST TYFKKTSIQMWNHIRGPPY
N33_67811_TranslatedLonge N33_67891011_TranslatedLo N33_678911_TranslatedLong N33_611_TranslatedLongest N33_68+911_TranslatedLong N33_68+11_TranslatedLonge	AHKNPHNGQVSYIHGSSQAQFVAESHÜL KAAFTHEMULLNEAATSKG AHKNPHNGQVSYIHGSSQAQFVAESHÜL KAAFTHEMULLNEAATSKG AHKNPHNGQVSYIHGSSQAQFVAESHÜL KAAFTHEMULLNEAATSKG AHKNPHNGQV AHKNPHNGQVFNHSGTLCSEPEKLIDFIHIYVYGFLDNYCRCRY AHKNPHNGQVFNHSGTLCSEPEKLIDFIHIYVYGFLDNYCRCRY
N33_67811_TranslatedLonge N33_67891011_TranslatedLo N33_678911_TranslatedLong N33_611_TranslatedLongest N33_68+911_TranslatedLong N33_68+11_TranslatedLonge	DVGKRR

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Figure 10

Published GRIK4 nucleic acid sequence (accession NM 014619).

```
1 atgccccgcg tctcggcgcc tttggtgctg cttcctgcgt ggctcgtgat ggtcgcctqc
  61 agcccgcact ccttgaggat cgctgctatc ttggacgacc ccatggagtg cagcagagg
 121 gageggetet ecateaceet ggecaagaac egeateaace gegeteetga gaggetggge
 181 aaggccaagg tcgaagtgga catctttgag cttctcagag acagcgagta cgagactgca
 241 gaaaccatgt gtcagatcct ccccaagggg gtggtcgctg tcctcggacc atcgtccagc
 301 ccagceteca getecateat cagcaacate tgtggagaga aggaggtece teaetteaaa
 361 gtggccccag aggagttcgt caagttccag ttccagagat tcacaaccct qaacctccac
 421 cccagcaaca ctgacatcag cgtggctgta gctgggatcc tgaacttctt caactgcacc
 481 accgcctgcc tcatctgtgc caaagcagaa tgccttttaa acctagagaa gctgctccqq
 541 caatteetta tetecaagga caegetgtee gteegeatge tggatgacae eegggaceee
 601 acceegetee teaaggagat eegggaegae aagacegeea ceateateat eeaegeeaae
 661 gcctccatgt cccacaccat cctcctgaag gcagccgaac ttgggatggt gtcagcctat
 721 tacacataca tottcactaa totggagtto toactocaga gaacggacag cottgtggat
 781 gategtgtca acatectggg attttccatt ttcaaccaat cccatgettt ettccaagag
 841 tttgcccaga gcctcaacca gtcctggcag gagaactgtg accatgtgcc cttcactggg
 901 cetgegetet ceteggeeet getgtttgat getgtetatg etgtggtgae tgeggtgeag
 961 gaactgaacc ggagccaaga gatcggcgtg aagcccttgt cctgcggctc ggcccagatc
1021 tggcagcacg gcaccagcct catgaactac ctgcgcatgg tagaattgga aggtcttacc
1081 ggccacattg aattcaacag caaaggccag aggtccaact acgctttgaa aatcttacag
1141 ttcacaagga atggttttcg gcagatcggc cagtggcacg tggcagaggg cctcagcatg
1201 gacagecace tetatgeete caacateteg gacactetet teaacaceae cetggtegte
1261 accaccatcc tggaaaaccc atatttaatg ctgaagggga accaccagga gatggaaggc
1321 aatgaccgct acgagggctt ctgtgtggac atgctcaagg agctggcaga gatcctccga
1381 ttcaactaca agatccgcct ggttggggat ggcgtgtacg gcgttcccga ggccaacggc
1441 acctggacgg gaatggtcgg ggagctgatc gctaggaaag cagatctggc tgtggcaggc
1501 ctcaccatta cagctgaacg ggagaaggtg attgatttct ctaagccatt catgactctg
1561 ggaattagca ttetttaccg catteatatg ggacgcaaac ceggetattt eteetteetq
1621 gacccatttt ctccgggcgt ctggctcttc atgcttctag cctatctggc cgtcagctgt
1681 gtcctcttcc tggtggctcg gttgacgccc tacgagtggt acagcccaca cccatgtgcc
1741 cagggeeggt geaaceteet ggtgaaceag tacteeetgg geaacageet etggttteeg
1801 gtcggggggt tcatgcagca gggctccacc atcgcccctc gcgccttatc cacccgctgt
1861 gtcagtggcg tctggtgggc attcacgctg atcatcatct catcctacac ggccaacctg
1921 gcagcettee tgacegtgca gegeatggat gtgcccattg agtcagtgga tgacetgget
1981 gaccagaccg ccattgaata tggcacaatt cacggaggct ccagcatgac cttcttccaa
2041 aatteeeget accagaceta ccaaegeatg tggaattaca tgtatteeaa geageeeage
2101 gtgttcgtga agagcacaga ggagggaatc gccagggtgt tgaattccaa ctacgccttc
2161 ctcctggaat ccaccatgaa cgagtactat cggcagcgaa actgcaacct cactcagatt
2221 gggggcctgc tggacaccaa gggctatggg attggcatgc cagtcggctc ggttttccgg
2281 gacgagtttg atctggccat tctccagctg caggagaaca accgcctgga gatcctgaag
2341 cgcaaatggt gggaaggagg gaagtgccc aaggaggaag atcacaqaqc taaaqqcctq
2401 ggaatggaga atattggtgg aatctttgtg gttcttattt gtggcttaat cgtggccatt
2461 tttatggcta tgttggagtt tttatggact ctcagacact cagaagcaac tgaggtgtcc
2521 gtctgccagg agatggtgac cgagctgcgc agcattatcc tgtgtcagga cagtatccac
2581 ccccgccggc ggcgccgc agtcccgccg ccccggcccc ccatccccga ggagcgccga
2641 ccgcggggca cggcgacgct cagcaacggg aagctgtgcg gggcagggga gcccgaccag
2701 etegegeaga gactggegea ggaggeegee etggtggeee geggetgeae geacateege
2761 gtctgccccg agtgccgccg cttccagggc ctgcgggcac ggccgtcgcc cgcccgcagc
2821 gaggagagcc tggagtggga gaaaaccacc aacagcagcg agcccgagta g
```

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Figure 11

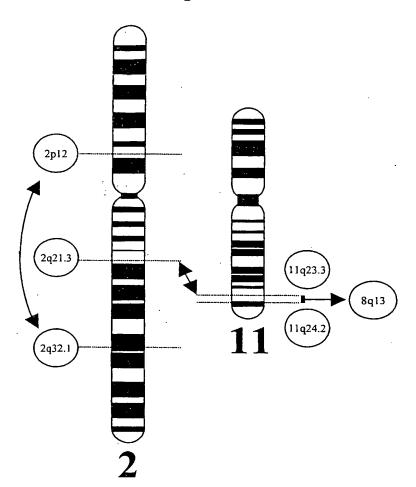
Published GRIK4 protein sequence (accession NP_055434).

MPRVSAPLVLLPAWLVMVACSPHSLRIAAILDDPMECSRGERLSITLAKNRINRAPERL GKAKVEVDIFELLPDSEYETAETMCQILPKGVVAVLGPSSSPASSSIISNICGEKEVPH FKVAPEEFVKFQFQRFTTLNLHPSNTDISVAVAGILNFFNCTTACLICAKAECLLNLEK LLRQFLISKDTLSVRMLDDTRDPTPLLKEIRDDKTATIIIHANASMSHTILLKAAELGM VSAYYTYIFTNLEFSLQRTDSLVDDRVNILGFSIFNQSHAFFQEFAQSLNQSWQENCDH VPFTGPALSSALLFDAVYAVVTAVQELNRSQEIGVKPLSCGSAQIWQHGTSLMNYLRMV ELEGLTGHIEFNSKGQRSNYALKILQFTRNGFRQIGQWHVAEGLSMDSHLYASNISDTL FNTTLVVTTILENPYLMLKGNHQEMEGNDRYEGFCVDMLKELAEILRFNYKIRLVGDGV YGVPEANGTWTGMVGELIARKADLAVAGLTITAEREKVIDFSKPFMTLGISILYRIHMG RKPGYFSFLDPFSPGVWLFMLLAYLAVSCVLFLVARLTPYEWYSPHPCAQGRCNLLVNQ YSLGNSLWFPVGGFMQQGSTIAPRALSTRCVSGVWWAFTLIIISSYTANLAAFLTVQRM DVPIESVDDLADQTAIEYGTIHGGSSMTFFQNSRYQTYQRMWNYMYSKQPSVFVKSTEE GIARVLNSNYAFLLESTMNEYYRQRNCNLTQIGGLLDTKGYGIGMPVGSVFRDEFDLAI LQLQENNRLEILKRKWWEGGKCPKEEDHRAKGLGMENIGGIFVVLICGLIVAIFMAMLE FLWTLRHSEATEVSVCQEMVTELRSIILCQDSIHPRRRRAAVPPPRPPIPEERRPRGTA TLSNGKLCGAGEPDQLAQRLAQEAALVARGCTHIRVCPECRRFOGLRARPSPARSEESL EWEKTTNSSEPE

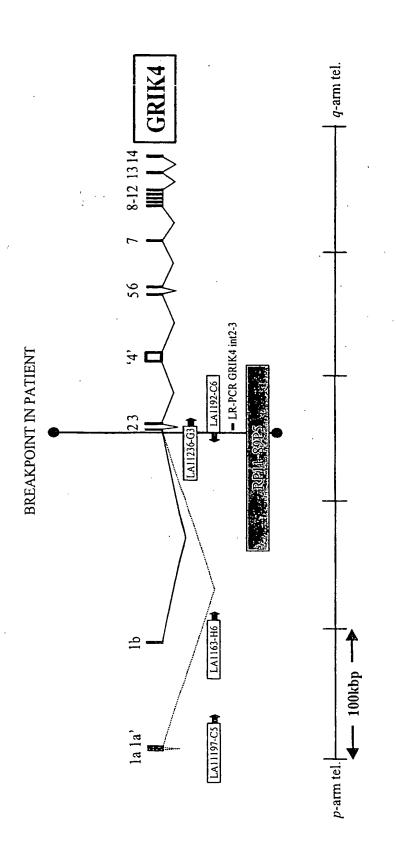
Figure 12

Cytogenetic Position	Description	Breakpoint YAC Clones	Breakpoint BAC Clones (Acc. No.)
2p12	Inversion breakpoint	915 f 7	-
2q32.1	Inversion breakpoint	941_h_12	RP11-358M9 (AC020595)
2q21.3	Translocation breakpoint	766_c_12	RP11-250H22 (AC011996)
11q23.3	Upper insertion breakpoint	936_d_9	RP11-89P5 (AC009641)
11q24.2	Translocation/Insertion breakpoint	749_d_2	RP11-687M24 (AP001007)

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Figure 15

Exon la

GCGTGGTAGCATGTCCTGTAATCCCAGTGCTTTGGGACACCGAGGCAGGAGGATCACT CGAGCCCAGGAGTGCGAGGCTGCAgtgagttatgatcatac

Exon la'

M E A K A

Exon 1b

Exon 2

 $\begin{array}{ccccccc} \texttt{gaaaccccccaq} \texttt{CTGCTATCTTGGACGACCCCATGGAGTGCAGCAGAGGGGAGCGGC} \\ & \texttt{A} & \texttt{I} & \texttt{L} & \texttt{D} & \texttt{D} & \texttt{P} & \texttt{M} & \texttt{E} & \texttt{C} & \texttt{S} & \texttt{R} & \texttt{G} & \texttt{E} & \texttt{R} & \underline{\texttt{L}} \\ \texttt{TCTCCATCACCCTGGCCAAGAACCGCATCAACCGCGCTCCTGAGAGGCTGGGCAAGGCC} \\ & \texttt{S} & \texttt{I} & \texttt{T} & \texttt{L} & \texttt{A} & \texttt{K} & \texttt{N} & \texttt{R} & \texttt{I} & \texttt{N} & \texttt{R} & \texttt{P} & \texttt{E} & \texttt{R} & \texttt{L} & \texttt{G} & \texttt{K} & \texttt{A} \\ & \texttt{AAGGTCGAAGTGGACATCTTTGAGCTTCTCAGAGACAGCGAGTACGAGACTGCAGAAAC} \\ & \texttt{K} & \texttt{V} & \texttt{E} & \texttt{V} & \texttt{D} & \texttt{I} & \texttt{F} & \texttt{E} & \texttt{L} & \texttt{L} & \texttt{R} & \texttt{D} & \texttt{S} & \texttt{E} & \texttt{Y} & \texttt{E} & \texttt{T} & \texttt{A} & \texttt{E} & \texttt{T} \\ \end{array}$

CAgtacgtagactggg M

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Figure 16

Alternative nucleic acid sequence. Exons la-la'-2-etc.

```
1 gegtggtage atgtgeetgt aateceagtg etttgggaca eegaggeagg aggateaete
   61 gageccagga gtgcgagget gcagtgacge tagaettcag gaagacceec catttetget
  121 ccactcctgg gcttggagaa gagtacagct gctcttgact ggtgggacct tttgctggct
  181 aggggtgatg ggagaagcaa gagagggato cacacacctg cgottagott totatgacct
  241 gggcggatgg aggccaaagc tgctatcttg gacgacccca tggagtgcag. cagaggggag
  301 cggctctcca tcaccetggc caagaaccgc atcaaccgcg ctcctgagag gctgggcaag
  361 gccaaggteg aagtggacat ctttgagett etcagagaca gegagtaega gactgeagaa
  421 accatgtgtc agatectece caagggggtg gtegetgtec teggaceate gtecageeca
  481 gcctccagct ccatcatcag caacatctgt ggagagaagg aggtccctca cttcaaagtg
  541 gccccagagg agttcgtcaa gttccagttc cagagattca caaccctgaa cctccacccc
  601 agcaacactg acatcagcgt ggctgtagct gggatcctga acttcttcaa ctgcaccacc
  661 gcctgcctca tctqtqccaa aqcaqaatgc cttttaaacc tagagaagct gctccggcaa
  721 ttccttatct ccaaggacac getgteegte egeatgetgg atgacaceeg ggaceeeace
  781 cegetectea aggagatecg ggacgacaag acegecacea teateateca egecaaegee
 841 tecatgtece acaccatect cetgaaggea geegaacttg ggatggtgte ageetattae
 901 acatacatet teactaatet ggagttetea etecagagaa eggacageet tgtggatgat
  961 cgtgtcaaca tcctgggatt ttccattttc aaccaatccc atgctttctt ccaagagttt
 1021 gcccagagcc tcaaccagtc ctggcaggag aactgtgacc atgtgccctt cactgggcct
 1081 gegeteteet eggeeetget gtttgatget gtetatgetg tggtgactge ggtgeaggaa
 1141 ctgaaccgga gccaagagat cggcgtgaag cccttgtcct gcggctcggc ccagatctgg
 1201 cagcacggca ccagceteat gaactacetg egeatggtag aattggaagg tettacegge
 1261 cacattgaat tcaacagcaa aggccagagg tccaactacg ctttgaaaat cttacagttc
 1321 acaaggaatg gtttteggca gateggeeag tggcaegtgg cagagggeet cageatggae
 1381 agccacctct atgcctccaa catctcggac actctcttca acaccaccct ggtcgtcacc
 1441 accatcctgg aaaacccata tttaatgctg aaggggaacc accaggagat ggaaggcaat
 1501 gaccgctacg agggcttctg tgtggacatg ctcaaggagc tggcagagat cctccgattc
 1561 aactacaaga teegeetggt tggggatgge gtgtaeggeg tteeegagge caaeggeace
 1621 tggacgggaa tggtcgggga gctgatcgct aggaaagcag atctggctgt ggcaggcctc
 1681 accattacag ctgaacggga gaaggtgatt gatttctcta agccattcat gactctggga
1741 attagcattc tttaccgcat tcatatggga cgcaaacccg gctatttctc cttcctggac
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 1981 ggggggttca tgcagcaggg ctccaccatc gcccctcgcg ccttatccac ccgctgtgtc
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 2161 cagaccgcca ttgaatatgg cacaattcac ggaggctcca gcatgacctt cttccaaaat
 2221 tecegetace agacetacea aegeatgtgg aattacatgt attecaagea geecagegtg
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 2341 ctggaatcca ccatgaacga gtactatcgg cagcgaaact gcaacctcac tcagattggg
 2401 ggcctgctgg acaccaaggg ctatgggatt ggcatgccag tcggctcggt tttccgggac
 2461 gagtttgatc tggccattct ccagctgcag gagaacaacc gcctggagat cctgaagcgc
 2521 aaatggtggg aaggagggaa gtgccccaag gaggaagatc acagagctaa aggcctggga
 2581 atggagaata ttggtggaat ctttgtggtt cttatttgtg gcttaatcgt ggccattttt
 2641 atggctatgt tggagttttt atggactete agacaeteag aagcaaetga ggtgteegte
 2701 tgccaggaga tggtgaccga gctgcgcagc attatcctgt gtcaggacag tatccaccc
 2761 egeoggegge gegeegeagt eeegeegeee eggeeeeea teeeegagga gegeegaeeg
 2821 cggggcacgg cgacgctcag caacgggaag ctgtgcgggg caggggagcc cgaccagctc
 2881 gcgcagagac tggcgcagga ggccgcctg gtggcccgcg gctgcacgca catccgcgtc
 2941 tgccccgagt gccgccgctt ccagggcctg cgggcacggc cgtcgcccgc ccgcagcgag
 3001 gagagcetgg agtgggagaa aaccaccaac agcagcgage ccqaqtaq
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WO 03/087408

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Figure 17

Complete alternative protein sequence

MEAKAAILDDPMECSRGERLSITLAKNRINRAPERLGKAKVEVDIFELLRDSEYETAET MCQILPKGVVAVLGPSSSPASSSIISNICGEKEVPHFKVAPEEFVKFQFQRFTTLNLHP SNTDISVAVAGILNFFNCTTACLICAKAECLLNLEKLLRQFLISKDTLSVRMLDDTRDP TPLLKEIRDDKTATIIIHANASMSHTILLKAAELGMVSAYYTYIFTNLEFSLQRTDSLV DDRVNILGFSIFNQSHAFFQEFAQSLNQSWQENCDHVPFTGPALSSALLFDAVYAVVTA VQELNRSQEIGVKPLSCGSAQIWQHGTSLMNYLRMVELEGLTGHIEFNSKGQRSNYALK ILQFTRNGFRQIGQWHVAEGLSMDSHLYASNISDTLFNTTLVVTTILENPYLMLKGNHO EMEGNDRYEGFCVDMLKELAEILRFNYKIRLVGDGVYGVPEANGTWTGMVGELIARKAD LAVAGLTITAEREKVIDFSKPFMTLGISILYRIHMGRKPGYFSFLDPFSPGVWLFMLLA YLAVSCVLFLVARLTPYEWYSPHPCAQGRCNLLVNQYSLGNSLWFPVGGFMQQGSTIAP RALSTRCVSGVWWAFTLIIISSYTANLAAFLTVQRMDVPIESVDDLADQTAIEYGTIHG GSSMTFFQNSRYQTYQRMWNYMYSKQPSVFVKSTEEGIARVLNSNYAFLLESTMNEYYR QRNCNLTQIGGLLDTKGYGIGMPVGSVFRDEFDLAILQLQENNRLEILKRKWWEGGKCP KEEDHRAKGLGMENIGGIFVVLICGLIVAIFMAMLEFLWTLRHSEATEVSVCQEMVTEL RSIILCQDSIHPRRRRAAVPPPRPPIPEERRPRGTATLSNGKLCGAGEPDQLAQRLAQE AALVARGCTHIRVCPECRRFQGLRARPSPARSEESLEWEKTTNSSEPE

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Figure 18

NPAS3 (NM_022123) nucleic acid sequence (spliceform 1b-3-4etc)

1 ccacgcgtcc gacgccccc acccgggagg ggggagagag gcaaaaagta agagaggaaa 61 aaaaatagca ggaagatggc goccaccaag cocagottto agcaggatco ttocaggoga . 121 gaacgtttac aagcattgag aaaggagaaa tcccgagatg ctgctcgctc ccqccqqqqa 181 aaagaaaact ttgagttcta tgaattggcc aagttgttgc ctcttcctgc agccattacc 241 agccageteg acaaggeate cateattega ettacaatta getatetgaa aatgagggae 301 tttgctaacc agggggaccc tccgtggaac ttgcgaatgg aaggccctcc acctaacaca 361 tcagtaaaag gtgcacagcg aaggagaagc cccagtgcac tagccattga agtatttgaa 421 gcacatttgg gaagccacat tttgcagtcc ctggatggct ttgtatttgc actaaatcag 481 gaaggaaaat ttttgtacat ttccgaaaca gtctccatct acctaggcct ctcacaaqtq 541 gagetgacag geageagtgt etttgaetat gteeaceeeg gagateaegt ggagatgget 601 gagcagetgg geatgaaget eeeceetggg eggggtetee tgteacaggg eaetgetgag 661 gacggagcca gctcagcatc ttcctcctct cagtcggaga cccccgagcc agtggagtca 721 accagececa gtetgetaac caetgacaac actettgage gtteettttt cateegaatg 781 aaatctactc tgaccaaacg cggtgtgcac atcaaatcat caggatataa ggtgattcac 841 ataacaggcc ggctacgcct gagagtgtcg ctgtcccacg ggaggaccgt ccccagccaa 901 atcatgggtc tcgtggttgt tgcgcatgcc ttgcctcccc ctacgatcaa tgaagtcaga 961 attgactgcc atatgttcgt cactcgagta aatatggacc tcaatatcat ttactgtgaa 1021 aataggatta gtgattatat ggatctgacc cctgtagata tcgtagggaa gagatgctac 1081 cacticatec atgetgaaga egtggaggge ateaggeaca gteaettgga ettgetgaat 1141 aagggtcagt gtgtgacaaa gtactatcgc tggatgcaga agaacggagg atatatttgg 1201 atacagteca gtgccaccat agetattaat gccaagaatg caaatgaaaa gaatateate 1261 tgggtgaatt accttcttag caatcctgag tacaaggaca cacccatgga catcgcacag 1321 ctcccccatc tgccggagaa aacttccgaa tcctcggaga catccgactc tgagtcagac 1381 tetaaagaca ceteaggtat tacagaggac aacgagaact ceaagteega egagaagggg 1441 aaccagteeg agaacagega agaceeggag eeeggeegga agaagteggg caaegegtgt 1501 gacaacgaca tgaactgcaa cgacgacggc cacagctcca gtaacccgga cagccgcgac 1561 agcgacgaca gettegagea eteggaettt gagaacecea aggegggega ggaeggette 1621 ggtgctctgg gcgcgatgca gatcaaggtg gagcgctacg tggagagcga gtcggacctq 1681 eggetgeaga actgegagte acteaegtee gacagegeea aggactegga cagegeagge 1741 gaggcgggcg cgcaggcctc cagcaagcac cagaagcgca agaaaaggcg gaaacggcaa 1801 aagggeggea gegeeageeg eeggegeetg teeagegegt egageeeagg eggeetggae 1861 gegggeetgg tggageecee geggetgetg teeteeceea acagtgeete ggtgeteaaq 1921 atcaagacgg agateteaga acceateaat ttegacaatg acageageat etggaactae 1981 ccgcccaacc gggagatete caggaacgag teccectaca geatgaccaa geececcage 2041 tetgageact tecegteece geagggegge ggeggtgggg gtggeggtgg eggggggetg 2101 caegtggcca ttecegaete ggteeteaee eegeeeggeg eegaeggege ggeegeeege 2161 aagactcagt teggegeete ggecaeegeg geeetggeee eegtegeete egaeeegetg 2281 ggcggggcg gcggcgggg gggcggcggc cccagcgcgt ccaactcctt gctgtacact 2341 ggggacctgg aggcgctgca gaggttgcag gcgggcaacg tcgtgctccc gctggtgcac 2401 agggtgaccg ggaccctggc cgccaccagc acggccgcgc agagggtcta caccacgggc 2461 accatccgct acgcgcccgc cgaggtgacc ctggccatgc agagcaacct gctgcccaac 2521 gegeacgetg ttaacttegt ggacgttaac ageceegget ttggeetega eeccaagacq 2581 cccatggaga tgctctacca ccacgtgcac cggctcaaca tgtcaggacc gttcggcggc 2641 gcagtgagcg cagctagcct gacgcagatg cccgccggca acgtgttcac cacggccgag 2701 ggactettet ceaegetgee etteceegte tacageaacg geatecaege ggeacagaet 2761 ctggagcgca aggaggactg aggcgccgcc cgtcctgggc ccggccaqqc cccqcttqqa 2821 ggaggcatcg tcggcatttt cgtttagacc tttaattcta gcactttgaa ttcgagcagg

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```
2881 tcagcgtctt ctetcgccac gacggtcccc attccacccc ctetttett cacctgactt 2941 attettegt gtaaagatat gtttatttt tgeettcaga gggtcagacg accagttgcc 3001 tgeegttttg tettetta aggtgtgtt tgggttgtt tgettteett tgeatettta 3061 ttaagatgte tttcatgtgt atatgeetet geeatagaat acteagtett gtggtcaaga 3121 gagttetcaa gtgacaacca ttggggttte tteataaaga tettgatatg ateaagatgg 3181 aaagagacaa gcataaacaa tgtgeetett ttgactaagt caaatgaaat agggtggttt 3241 ttgtttetgt teetaattee tttaaaaaat agggggaata gtattttaga attttatgea 3301 gaatttaatt etettttae ggttaagatt ttaagatttt ettaettgea cataaaaata 3361 atttgggtte ttaaacttaa tttetggeet gtgactagaa tgtttaaaaa aaaaaaaaac 3421 eetegtge
```

Figure 19

NPAS3 protein sequence (spliceform 1b-3-4etc.)

MAPTIKESFOODPSREERLQALRKEKSRDAARSRRGKENFEFYELAKLLPLPAAITSQLD KASIIRLTISYLKMRDFANQGDPPWNLRMEGPPPNTSVKGAQRRRSPSALAIEVFEAHL GSHILQSLDGFVFALNQEGKFLYISETVSIYLGLSQVELTGSSVFDYVHPGDHVEMAEQ LGMKLPPGRGLLSQGTAEDGASSASSSSQSETPEPVESTSPSLLTTDNTLERSFFIRMK STLTKRGVHIKSSGYKVIHITGRLRLRVSLSHGRTVPSQIMGLVVVAHALPPPTINEVR IDCHMFVTRVNMDLNIIYCENRISDYMDLTPVDIVGKRCYHFIHAEDVEGIRHSHLDI. NKGQCVTKYYRWMQKNGGYIWIQSSATIAINAKNANEKNIIWVNYLLSNPEYKDTPMDI AQLPHLPEKTSESSETSDSESDSKDTSGITEDNENSKSDEKGNOSENSEDPEPDRKKSG NACDNDMNCNDDGHSSSNPDSRDSDDSFEHSDFENPKAGEDGFGALGAMQIKVERYVES ESDLRLQNCESLTSDSAKDSDSAGEAGAQASSKHQKRKKRRKRQKGGSASRRRLSSASS PGGLDAGLVEPPRLLSSPNSASVLKIKTEISEPINFDNDSSIWNYPPNREISRNESPYS MTKPPSSEHFPSPQGGGGGGGGGGLHVAI PDSVLTPPGADGAAARKTQFGASATAALA PVASDPLSPPLSASPRDKHPGNGGGGGGGGGGGGGGGGPSASNSLLYTGDLEALQRLQAG NVVLPLVHRVTGTLAATSTAAQRVYTTGTIRYAPAEVTLAMOSNLLPNAHAVNFVDVNS PGFGLDPKTPMEMLYHHVHRLNMSGPFGGAVSAASLTOMPAGNVFTTAEGLFSTLPFPV YSNGIHAAOTLERKED

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Figure 20

NPAS3 nucleic acid sequence (spliceform incorporating exons 1a-2-3-4etc) similar to mouse cDNA with accession number NM_013780)

. —	,13,00,					
1	ATGGGGAGGG	CCGGCGCCGC	GGCCAACGGC	ACCCCGCAGA	ACGTCCAGGG	CATCACCTCC
51	TACCAGCAGC	GAATAACTGC	CCAGCATCCT	CTGCCCAACC	AATCAGAATG	TAGGAAAATC
121	TACAGATATG	ACGGAATCTA	CTGTGAATCT	ACCTACCAGA	ATTTACAAGC	ATTGAGAAAG
181	GAGAAATCCC	GAGATGCTGC	TCGCTCCCGC	CGGGGAAAAG	AAAACTTTGA	GTTCTATGAA
241	TTGGCCAAGT	TGTTGCCTCT	TCCTGCAGCC	ATTACCAGCC	AGCTCGACAA	GGCATCCATC
301	ATTCGACTTA	CAATTAGCTA	TCTGAAAATG	AGGGACTTTG	CTAACCAGGG	GGACCCTCCG
361	TGGAACTTGC	GAATGGAAGG	CCCTCCACCT	AACACATCAG	TAAAAGGTGC	ACAGCGAAGG
421	AGAAGCCCCA	GTGCACTAGC	CATTGAAGTA	TTTGAAGCAC	ATTTGGGAAG	CCACATTTTG
481	CAGTCCCTGG	ATGGCTTTGT	ATTTGCACTA	AATCAGGAAG	GAAAATTTTT	GTACATTTCC
541	GAAACAGTCT	CCATCTACCT	AGGCCTCTCA	CAAGTGGAGC	TGACAGGCAG	CAGTGTCTTT
			TCACGTGGAG			
661	CCTGGGCGGG	GTCTCCTGTC	ACAGGGCACT	GCTGAGGACG	GAGCCAGCTC	AGCATCTTCC
721	TCCTCTCAGT	CGGAGACCCC	CGAGCCAGTG	GAGTCAACCA	GCCCCAGTCT	GCTAACCACT
781	GACAACACTC	TTGAGCGTTC	CTTTTTCATC	CGAATGAAAT	CTACTCTGAC	CAAACGCGGT
841	GTGCACATCA	AATCATCAGG	ATATAAGGTG	ATTCACATAA	CAGGCCGGCT	ACGCCTGAGA
901	GTGTCGCTGT	CCCACGGGAG	GACCGTCCCC	AGCCAAATCA	TGGGTCTCGT	GGTTGTTGCG
961	CATGCCTTGC	CTCCCCCTAC	GATCAATGAA	GTCAGAATTG	ACTGCCATAT	GTTCGTCACT
1021	CGAGTAAATA	TGGACCTCAA	TATCATTTAC	TGTGAAAATA	GGATTAGTGA	TTATATGGAT
1081	CTGACCCCTG	TAGATATCGT	AGGGAAGAGA	TGCTACCACT	TCATCCATGC	TGAAGACGTG
1141	GAGGGCATCA	GGCACAGTCA	CTTGGACTTG	CTGAATAAGG	GTCAGTGTGT	GACAAAGTAC
1201	TATCGCTGGA	TGCAGAAGAA	CGGAGGATAT	ATTTGGATAC	AGTCCAGTGC	CACCATAGCT
1261	ATTAATGCCA	AGAATGCAAA	TGAAAAGAAT	ATCATCTGGG	TGAATTACCT	TCTTAGCAAT
1321	CCTGAGTACA	AGGACACACC	CATGGACATC	GCACAGCTCC	CCCATCTGCC	GGAGAAAACT
1381	TCCGAATCCT	CGGAGACATC	CGACTCTGAG	TCAGACTCTA	AAGACACCTC	AGGTATTACA
1441	GAGGACAACG	AGAACTCCAA	GTCCGACGAG	AAGGGGAACC	AGTCCGAGAA	CAGCGAAGAC
1501	CCGGAGCCCG	ACCGGAAGAA	GTCGGGCAAC	GCGTGTGACA	ACGACATGAA	CTGCAACGAC
1561	GACGGCCACA	GCTCCAGTAA	CCCGGACAGC	CGCGACAGCG	ACGACAGCTT	CGAGCACTCG
1621	GACTTTGAGA	ACCCCAAGGC	GGGCGAGGAC	GGCTTCGGTG	CTCTGGGCGC	GATGCAGATC
1681	AAGGTGGAGC	GCTACGTGGA	GAGCGAGTCG	GACCTGCGGC	TGCAGAACTG	CGAGTCACTC
1741	ACGTCCGACA	GCGCCAAGGA	CTCGGACAGC	GCAGGCGAGG	CGGGCGCGCA	GGCCTCCAGC
1801	AAGCACCAGA	AGCGCAAGAA	AAGGCGGAAA	CGGCAAAAGG	GCGGCAGCGC	CAGCCGCCGG
1861	CGCCTGTCCA	GCGCGTCGAG	CCCAGGCGGC	CTGGACGCGG	GCCTGGTGGA	GCCCCGCGG
1921	CTGCTGTCCT	CCCCCAACAG	TGCCTCGGTG	CTCAAGATCA	AGACGGAGAT	CTCAGAACCC
1981	ATCAATTTCG	ACAATGACAG	CAGCATCTGG	AACTACCCGC	CCAACCGGGA	GATCTCCAGG
2041	AACGAGTCCC	CCTACAGCAT	GACCAAGCCC	CCCAGCTCTG	AGCACTTCCC	GTCCCCGCAG
			CGGTGGCGGG			
2161	CTCACCCCGC	CCGGCGCCGA	CGGCGCGGCC	GCCCGCAAGA	CTCAGTTCGG	CGCCTCGGCC
2221	ACCGCGGCCC	TGGCCCCCGT	CGCCTCCGAC	CCGCTGTCAC	CCCCGCTCTC	GGCGTCCCCG
2281	CGGGACAAGC	ACCCCGGGAA	CGGCGGCGGG	GGCGGGGGCG	GGGGCGGCGG	CGCGGGGGGC
2341	GGCGGCCCCA	GCGCGTCCAA	CTCCTTGCTG	TACACTGGGG	ACCTGGAGGC	GCTGCAGAGG
			GCTCCCGCTG			
2461	ACCAGCACGG	CCGCGCAGAG	GGTCTACACC	ACGGGCACCA	TCCGCTACGC	GCCCGCCGAG
			CAACCTGCTG			
2581	GTTAACAGCC	CCGGCTTTGG	CCTCGACCCC	AAGACGCCCA	TGGAGATGCT	CTACCACCAC
2641	GTGCACCGGC	TCAACATGTC	AGGACCGTTC	GGCGGCGCAG	TGAGCGCAGC	TAGCCTGACG
2701	CAGATGCCCG	CCGGCAACGT	GTTCACCACG	GCCGAGGGAC	TCTTCTCCAC	GCTGCCCTTC
2761	CCCGTCTACA	GCAACGGCAT	CCACGCGGCA	CAGACTCTGG	AGCGCAAGGA	GGACTGAGGC
2821	GCCGCCCGTC	CTGGGCCCGG	CCAGGCCCCG	CTTGGAGGAG	GCATCGTCGG	CATTTTCGTT

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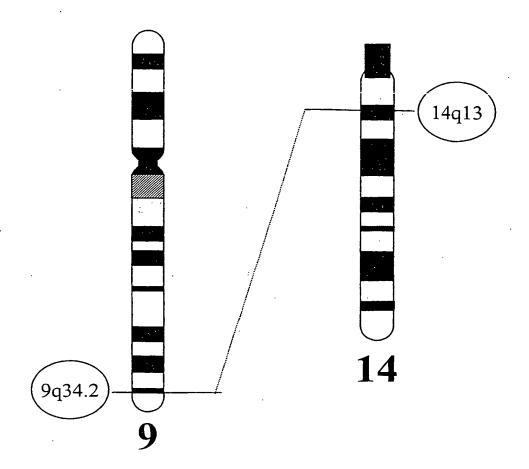
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Figure 21 .

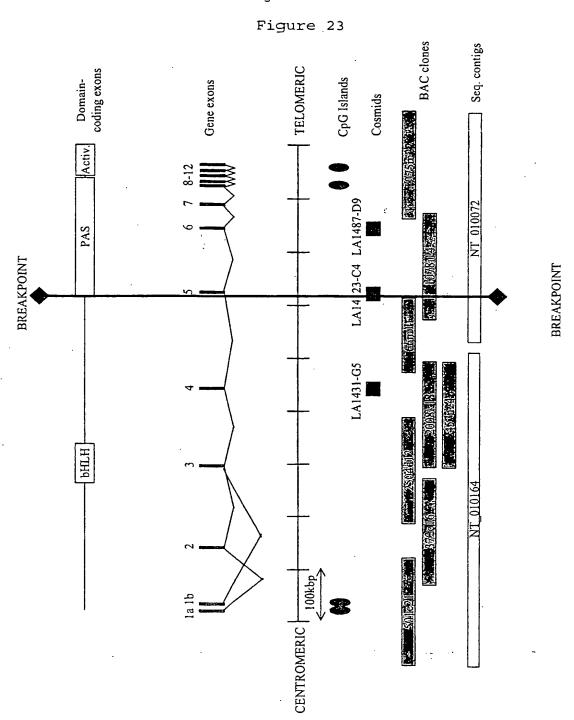
NPAS3 protein sequence of spliceform incorporating exons la-2-3-4etc.

MERACAAANGITEONWOOTHIS YOOTH TRAOLIDLENGS LECRELY EXDELY WEST YOUR OALR KEKSRDAARSRRGKENFEFYELAKLLPLPAAITSQLDKASIIRLTISYLKMRDFANQGD PPWNLRMEGPPPNTSVKGAQRRRSPSALAIEVFEAHLGSHILQSLDGFVFALNQEGKFL YISETVSIYLGLSQVELTGSSVFDYVHPGDHVEMAEQLGMKLPPGRGLLSQGTAEDGAS SASSSSQSETPEPVESTSPSLLTTDNTLERSFFIRMKSTLTKRGVHIKSSGYKVIHITG RLRLRVSLSHGRTVPSQIMGLVVVAHALPPPTINEVRIDCHMFVTRVNMDLNIIYCENR ISDYMDLTPVDIVGKRCYHFIHAEDVEGIRHSHLDLLNKGQCVTKYYRWMQKNGGYIWI QSSATIAINAKNANEKNIIWVNYLLSNPEYKDTPMDIAQLPHLPEKTSESSETSDSESD SKDTSGITEDNENSKSDEKGNQSENSEDPEPDRKKSGNACDNDMNCNDDGHSSSNPDSR DSDDSFEHSDFENPKAGEDGFGALGAMQIKVERYVESESDLRLONCESLTSDSAKDSDS AGEAGAQASSKHQKRKKRRKRQKGGSASRRRLSSASSPGGLDAGLVEPPRLLSSPNSAS VLKIKTEISEPINFDNDSSIWNYPPNREISRNESPYSMTKPPSSEHFPSPQGGGGGGG GGGLHVAIPDSVLTPPGADGAAARKTQFGASATAALAPVASDPLSPPLSASPRDKHPGN GGGGGGGGGGGGSASNSLLYTGDLEALQRLQAGNVVLPLVHRVTGTLAATSTAAO RVYTTGTIRYAPAEVTLAMQSNLLPNAHAVNFVDVNSPGFGLDPKTPMEMLYHHVHRLN MSGPFGGAVSAASLTQMPAGNVFTTAEGLFSTLPFPVYSNGIHAAQTLERKED

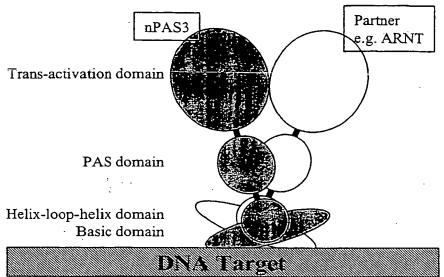
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Figure 22

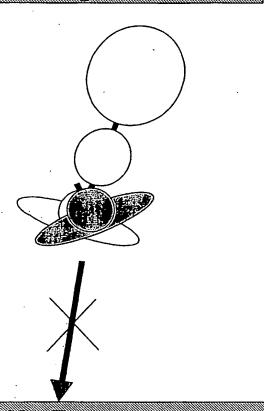


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Figure 24





DNA Target

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Figure 25 PDE4B1 (acc. L20966) Nucleic acid sequence

```
1 geggeegegg eggtgeagea gaggegeete gggeaggagg agggeggett etgegagge
  61 agcctgaggt attaaaaagt gtcagcaaac tgcattgaat aacagacatc ctaagagggg
 121 atattttcca cetetataat gaagaaaage aggagtgtga tgaeggtgat ggetgatgat
181 aatgttaaag attattttga atgtagettg agtaaateet acagttette cagtaacaca
241 cttgggatcg acctctggag agggagaagg tgttgctcag gaaacttaca gttaccacca
301 ctgtctcaaa gacagagtga aagggcaagg actcctgagg gagatggtat ttccaggccg
361 accacactgc ctttgacaac gcttccaagc attgctatta caactgtaag ccaggagtgc
421 tttgatgtgg aaaatggccc ttccccaggt cggagtccac tggatcccca ggccagctct
481 teegetggge tggtaettea egecacettt cetgggeaca gecagegeag agagteattt
541 ctctacagat cagacagcga ctatgacttg tcaccaaagg cgatgtcgag aaactcttct
601 cttccaagcg agcaacacgg cgatgacttg attgtaactc cttttgccca ggtccttgcc
661 agcttgcgaa gtgtgagaaa caacttcact atactgacaa accttcatgg tacatctaac
721 aagaggtccc cagctgctag tcagcctcct gtctccagag tcaacccaca agaagaatct
781 tatcaaaaat tagcaatgga aacgctggag gaattagact qqtqtttaga ccaqctagag
841 accatacaga cctaccggtc tgtcagtgag atggcttcta acaagttcaa aagaatgctg
901 aaccgggagc tgacacacct ctcagagatg agccgatcag ggaaccaggt gtctgaatac
961 atttcaaata ctttcttaga caagcagaat gatgtggaga tcccatctcc tacccagaaa
1021 gacagggaga aaaagaaaaa gcagcagctc atgacccaga taagtggagt gaagaaatta
1081 atgcatagtt caagcctaaa caatacaagc atctcacgct ttggagtcaa cactgaaaat
1141 gaagatcacc tggccaagga gctggaagac ctgaacaaat ggggtcttaa catctttaat
1201 gtggctggat attctcacaa tagaccccta acatgcatca tgtatgctat attccaggaa
1261 agagacetee taaagacatt cagaatetea tetgacacat ttataaceta catgatgact
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1381 gcccagtcga cccatgttct cctttctaca ccagcattag acgctgtctt cacagatttg
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1561 ttggaaaatc atcaccttgc tgtgggtttc aaactgctgg aagaagaaca ctgtgacatc
1621 ttcatgaatc tcaccaagaa gcagcgtcag acactcagga agatggttat tgacatggtg
1681 ttagcaactg atatgtctaa acatatgagc ctgctggcag acctgaagac aatggtagaa
1741 acgaagaag ttacaagttc aggcgttctt ctcctagaca actataccga tcgcattcag
1801 gtccttcgca acatggtaca ctgtgcagac ctgagcaacc ccaccaagtc cttggaattg
1861 tatcggcaat ggacagaccg catcatggag gaatttttcc agcagggaga caaagagcgg
1921 gagaggggaa tggaaattag cccaatqtgt gataaacaca cagcttctgt ggaaaaatcc
1981 caggttggtt tcatcgacta cattgtccat ccattgtggg agacatgggc agatttggta
2041 cagoctgatg ctcaggacat tctcgatacc ttagaagata acaggaactg gtatcagagc
2101 atgatacete aaagteeete aecaceaetg gaegageaga acagggaetg ceagggtetg
2161 atggagaagt ttcagtttga actgactctc gatgaggaag attctgaagg acctgagaag
2221 gagggagagg gacacagcta tttcagcagc acaaagacgc tttgtgtgat tgatccagaa
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2341 gatacataat ccccctctcc ctgtggagat gaacattcta tccttgatga gcatgccagc
2401 tatgtggtag ggccagccca ccatgggggc caagacctgc acaggacaag ggccacctgg
2461 cetttcagtt acttgagttt ggagtcagaa agcaagacca ggaagcaaat agcagctcag
2521 gaaatcccac ggttgacttg ccttgatggc aagcttggtg gagagggctg aagctgttgc
2581 tgggggccga ttctgatcaa gacacatggc ttgaaaatgg aagacacaaa actgagagat
2641 cattetgeae taagtttegg gaaettatee eegacagtga etgaaeteae tgaetaataa
2701 cttcatttat gaatettete acttgteeet ttgtetgeea acetgtgtge ettttttgta
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2821 acagataagc tttcaaagtt gacaaacttt tttgactctt tctggaaaaa ggaaagaaaa
2881 tagtetteet tetttettgg geaatateet teaetttaet acagttaett ttgeaaacag
2941 acagaaagga tacacttcta accacatttt acttccttcc cctgttgtcc agtccaactc
3001 cacagicact citaaaacti cictcigtti gcctgcctcc aacagiacti tiaactitti
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PCT/GB03/01543

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3061 gctgtaaaca gaataaaatt gaacaaatta gggggtagaa aggagcagtg gtgtcgttca 3121 ccgtgagagt ctgcatagaa ctcagcagtg tgccctgctg tgtcttggac cctgcaatgc 3181 ggccgc

Figure 26

PDE4B1 Protein sequence



QTYRSVSEMASNKFKRMLNRELTHLSEMSRSGNQVSEYISNTFLDKQNDVEIPSPTQKD REKKKKQQLMTQISGVKKLMHSSSLNNTSISRFGVNTENEDHLAKELEDLNKWGLNIFN VAGYSHNRPLTCIMYAIFQERDLLKTFRISSDTFITYMMTLEDHYHSDVAYHNSLHAAD VAQSTHVLLSTPALDAVFTDLEILAAIFAAAIHDVDHPGVSNQFLINTNSELALMYNDE SVLENHHLAVGFKLLQEEHCDIFMNLTKKQRQTLRKMVIDMVLATDMSKHMSLLADLKT MVETKKVTSSGVLLLDNYTDRIQVLRNMVHCADLSNPTKSLELYRQWTDRIMEEFFQQG DKERERGMEISPMCDKHTASVEKSQVGFIDYIVHPLWETWADLVQPDAQDILDTLEDNR NWYQSMIPQSPSPPLDEQNRDCQGLMEKFQFELTLDEEDSEGPEKEGEGHSYFSSTKTL CVIDPENRDSLGETDIDIATEDKSPVDT

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Figure 27

PDE4B3 (acc. U85048) Nucleic acid sequence

```
1 atgacagcaa aagattotto aaaggaactt actgottotg aacctgaggt ttgcataaag
 61 actttcaagg agcaaatgca tttagaactt gagcttccga gattaccagg aaacagacct
121 acatetecta aaatttetee aegeagttea eeaaggaact caccatgett ttteagaaag
181 ttactggtga ataaaagcat tcggcagcgt cgtcgcttca ctgtggctca tacatgcttt
241 gatgtggaaa atggcccttc cccaggtcgg agtccactgg atccccaggc cagctcttcc
301 getgggetgg taetteaege eacettteet gggeaeagee agegeagaga gteatttete
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2161 aca
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PCT/GB03/01543

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Figure 28

PDE4B3 Protein sequence



RMLNRELTHLSEMSRSGNQVSEYISNTFLDKQNDVEIPSPTQKDREKKKKQQLMTQISG VKKLMHSSSLNNTSISRFGVNTENEDHLAKELEDLNKWGLNIFNVAGYSHNRPLTCIMY AIFQERDLLKTFRISSDTFITYMMTLEDHYHSDVAYHNSLHAADVAQSTHVLLSTPALD AVFTDLEILAAIFAAAIHDVDHPGVSNQFLINTNSELALMYNDESVLENHHLAVGFKLL QEEHCDIFMNLTKKQRQTLRKMVIDMVLATDMSKHMSLLADLKTMVETKKVTSSGVLLL DNYTDRIQVLRNMVHCADLSNPTKSLELYRQWTDRIMEEFFQQGDKERERGMEISPMCD KHTASVEKSQVGFIDYIVHPLWETWADLVQPDAQDILDTLEDNRNWYQSMIPQSPSPPL DEQNRDCQGLMEKFQFELTLDEEDSEGPEKEGEGHSYFSSTKTLCVIDPENRDSLGETD IDIATEDKSPVDT

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Figure 29

PDE4B2 (acc. NM 002600) Nucleic acid sequence

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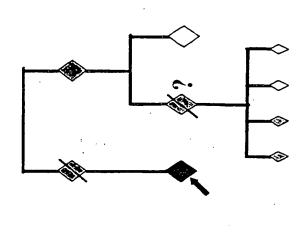
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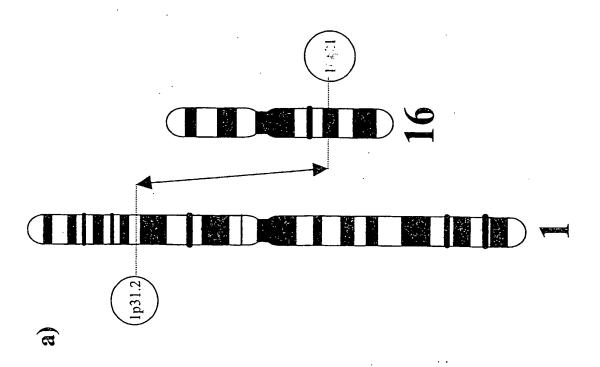
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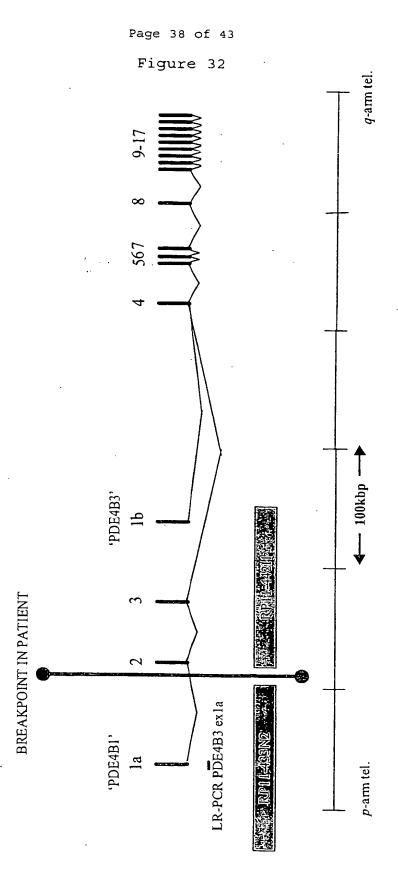
PDE4B2 Protein sequence

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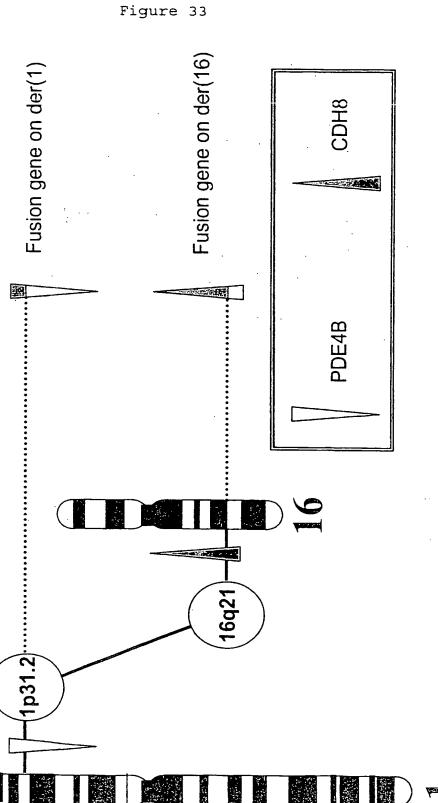
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Figure 31



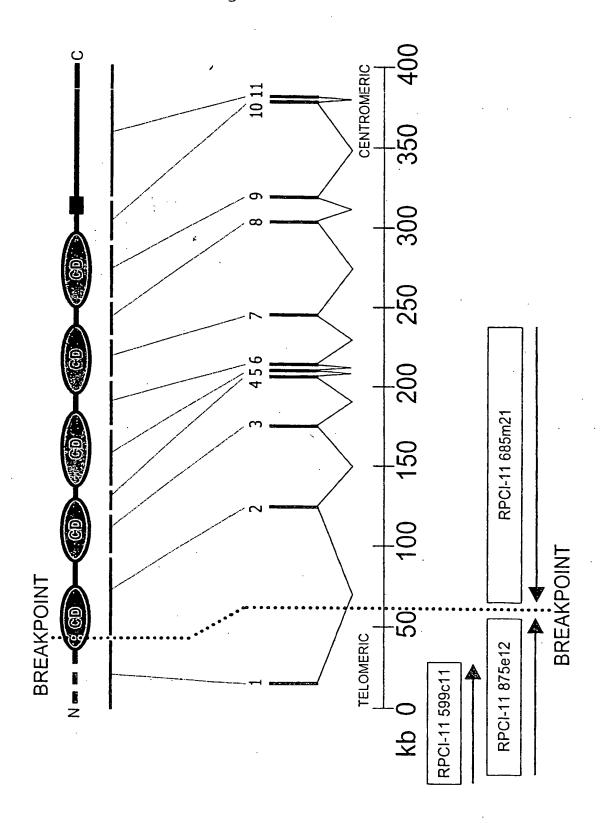




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Figure 34



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Figure 35

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Figure 36

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					GOLDEDNODG	EEQRILNRSK
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181	ILGTSVTNVT	ATDADDPVYG	NSAKLVYSIL	EGQPYFSIEP	ETAIIKTALP	NMDREAKEEY
241	<u>LVVIQAKD</u> MG	GHSGGLSGTT	TLTVTLTDVN	DNPPKFAQSL	YHFSVPEDVV	LGTAIGRVKA
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361	HIDPRFSGRG	PFKDTATVKI	VVEDADEPPV	FSSPTYLLEV	HENAALNSVI	GQVTARDPDI
421	TSSPIRFSID	RHTDLERQFN	INADDGKITL	ATPLDRELSV	WHNITIIATE	IRNHSQISRV
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541	NNPNFTIKKN	EDNSLSILAK	HNGFNRQKQE	VYLLPIIISD	SGNPPLSSTS	TLTIRVCGCS
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661	RENIIRYDDE	GGGEEDTEAF.	DIATLQNPDG	INGFLPRKDI	KPDLQFMPRQ	GLAPVPNGVD
721	VDEFINVRLH	EADNDPTAPP	YDSIQIYGYE	GRGSVAGSLS	SLESTTSDSD	QNFDYLSDWG
781	PREKRIGELY	SUGESDEET				

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Figure 37

a)

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